

CASE REPORT

Post-rotavirus vaccine intussusception in identical twins: A case report

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ABSTRACT

The intussusception is one of the most frequent causes of occlusive syndrome in infants and in children.¹ The mesenteric lymphadenopathy, which is very rare post rotavirus vaccination, can cause intussusception,²⁻⁵ especially in genetically predisposed individuals.⁶ There is an association between intussusception and some classes of genotype.⁷⁻⁹ Two infants aged 3 months, vaccinated against rotavirus. After about a week, one of the 2 identical infants presented inconsolable crying, vomiting, loose stools mixed with blood, and was diagnosed with bowel obstruction with intussusception. He was operated in urgency. After a few hours, his brother presented vomiting, and was admitted to our Hospital for suspected intussusception. The controls carried out have confirmed the presence of intussusception that was treated early, before the onset of severe symptoms. The incidence of post rotavirus vaccine intussusception is very low. The determining factor hypothetically might be linked to the presence of a genotype that exposes infants to a greater risk of developing mesenteric lymphadenitis and intussusception. In our case, the diagnosis of intussusception occurred in a twin, which allowed us to recognize early symptoms which accused the brother and schedule the surgery with less urgency. Our experience may want to sensitize families and pediatricians to report cases of intussusception given a theoretical familiar association. The study of the genotype could be decisive for or not to exclude the presence of a risk of invagination, thus avoiding vaccination.

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Background

The rotavirus (RV) is the leading cause of severe acute gastroenteritis in children worldwide^{1,2,3} and the most common cause of severe diarrhea in children aged under 5 y.^{4,5}

Before the introduction of the vaccine in the USA in 2006, rotavirus infection caused significant morbidity among U.S children, with an estimated 55,000–70,000 hospitalizations and 410,000 clinic visits annually.⁶ According to an analysis of 10 y of rotavirus infections in the USA before the introduction of the vaccine,⁷ rotavirus was estimated to be the cause of approximately 2.7 million (yes million) cases of severe gastroenteritis, 60,000 hospitalizations and 37 deaths annually. Because of the tremendous global burden of rotavirus, the World Health Organization (WHO) has prioritized vaccine development and introduction to control this disease. Recent data from both affluent and developing countries suggest that rotavirus vaccines are making a big difference in morbidity and especially mortality among children.⁸ Worldwide, more than 450,000 children under 5 y of age still die from rotavirus infection each year. Think about that—nearly one-half million children die from a disease that could be prevented by vaccine, every single year.⁹

The genome of rotavirus consists of 11 segments of double-stranded RNA which encode 6 viral proteins (VP). According to the different protein VP6 are distinguished 7 serogroups (AG), 3 of which are pathogenic for humans (A, B and C).

Serogroup A is the main responsible of RV gastroenteritis. The outer shell of the RV also contains the viral proteins VP7 and VP4. In the RV that infect humans have been identified at least 12 different VP7 antigens (G genotypes) and 15 VP4 (genotypes P).¹⁰ Currently 5 combinations GP (G1P, G2P, G3P, G4P and G9P)^{11,12} are responsible for 90% of all infections in humans RV in most of the world; serotype G1P¹¹ is the combination most frequently encountered.

The high epidemiological impact of rotavirus disease contrasts with the complete lack of preventive measures that are outside the vaccination. Large international premarketing and postmarketing studies have shown no serious adverse events associated with either rotavirus vaccine, and owing to the recommendations of the National Advisory Committee on Immunization,¹³ several countries have introduced a vaccine as part of their immunization program in the past 2 y. Of course, as is the case for all widely used vaccines, the safety profile and tolerability of vaccination against rotavirus remains under evaluation.

The first rotavirus vaccine (Rotashield) was licensed to trade in the US in 1998. Intussusception Rotashield-associated had a very low incidence (only 1 in 10 K vaccines), but this was judged to be higher than desired, hence, after 10 months, it was withdrawn.¹³ Currently, there are 2 vaccines against rotavirus: one monovalent (Rotarix[®]) derived from a live attenuated human strain which is administered in 2 doses by oral; one

pentavalent (RotaTeq[®]), consisting of a human bovine reassortant strain containing antigens G1, G2, G3, G4, and P, also be administered in 3 doses by oral. Both vaccines have shown to be effective in reducing cases of GARV. As regards the side effects, although in recent years several studies have revealed a significant increase of safety profile of such vaccines, the intestinal intussusception issue remains under study. Some recent results show that, although there was a significant reduction in cases of GARV, there has been a slight increase in cases of intussusception.¹⁵ The Yih study found a significant increase in the risk of intussusception after the first dose of Rotateq, with 1.5 excess cases per 100,000 vaccine recipients. They found no association with subsequent doses, but couldn't rule that out.¹⁶ For Rotarix, the findings were not significant, but a relatively small number of children got that vaccine (an order of magnitude lower), and the authors concluded that their risk estimates were imprecise and should be considered in the context of findings of increased risk in other studies.¹⁷ Their results should be considered along with other studies from the US and other countries. It is reasonable to conclude that intussusception can occur with either vaccine, but that the risk is low, on the order of 1-5 cases per 100,000 infants, therefore the benefit-risk balance for Rotarix[™] and RotaTeq[®] is favorable. From a public health perspective, the benefits in terms of prevented RVGE hospitalizations and deaths for the vaccinated population far exceed the estimated risks due to intussusception.^{18,19}

The pathophysiological mechanism of this type of intussusception hypothetically might be due to the action of rotavirus on the intestinal wall, in particular, the increase of the distal ileum wall thickness and the volume increase of the mesenteric lymphnodes.²⁰ The association between vaccination and intussusception has not traditionally been considered as an association which has a genetic basis. In recent years some authors have reported cases of idiopathic intussusception with hereditary predisposition.²¹ This hereditary predisposition, understood as anatomical alteration, could be considered as etiological factor in many cases of idiopathic intussusception. In these families with genetic predisposition, if there are triggers such as viral infections or as acquired immunity, intussusception would occur much more easily.

Case report

Two identical twins, both male, aged 3 months, born at term, in good health, in September 2014, on the advice of the pediatrician, have been vaccinated for the prevention of rotavirus gastroenteritis. Each twin received one dose of Rotarix[®] vaccine. After about one week after Rotarix[®] dose, one of the infants presented inconsolable crying, vomiting and stool mixed with blood. Arrived at our unit of pediatric surgery, it was diagnosed a bowel obstruction with intussusception and he was operated in urgency. A few hours after, the twin brother also presented vomiting, and was admitted to our Hospital for suspected intussusception. The controls carried out have confirmed the presence of intussusception. The diagnostic was carried out more rapidly than in the previous case report. The second twin was surgically treated early, before the onset of severe symptoms.

Discussion

The infants intussusception can be a surgical urgency and a significant commitment both to the pediatric surgeon that the anesthesiologist. It's one of the many causes of misdiagnosis and management problems in acute abdomen in children. Initial treatment, outside of some contraindications, it must have recourse to a radiological reduction: a pneumatic or hydrostatic barium under fluoroscopic control or, more recent technique, sonographically guided hydrostatic reduction with normal saline solution. The radiological reduction can be facilitated by an intravenous sedation. When the disease is not quickly diagnosed or radiological treatment fails, it is treated surgically, in the open or laparoscopically, with the consequent need to perform a general anesthesia and airway management, often in emergency. If intussusception is not treated at the right time, complications are ischemia, intestinal perforation and peritonitis. As with any other surgical pathology, a early diagnosis allows a more favorable surgical and anesthetic management in terms of patient outcome.

Rotavirus vaccination is a highly effective preventive measure against rotavirus gastroenteritis. The safety profile of such vaccines, which is generally excellent, remains under study, including for intussusception as a very rare serious AE. The contraindications to vaccination are currently represented by the presence of known hypersensitivity to the active substance or to any of the excipients; a history of intussusception or uncorrected congenital malformation of the gastrointestinal tract; severe combined immunodeficiency.²² A positive family history of intussusception in children was excluded from the contraindications. Although the homozygous assumes that the 2 brothers have the same genetic heritage, in our opinion, on the basis of some results in the literature and based on our clinical experience, even outside of cases of homozygosity, a family history of intussusception could lead to a early recognition of the symptoms, and then to the programming of surgery with less urgency.

Conclusions

Introduction of effective and available rotavirus vaccines has substantially affected worldwide deaths attributable to diarrhea. The findings in literature are consistent with the high field effectiveness of vaccination observed in post-licensure epidemiologic studies. Taken together, these findings reaffirm the large public health impact of routine rotavirus vaccination in reducing the circulation of rotavirus. New recent estimates can be used to advocate for rotavirus vaccine introduction and to monitor the effect of vaccination on mortality once introduced. We believe that further studies should be carried out to investigate the family predisposition to the disease. Waiting for scientific results in this regard, our experience may want to sensitize families and pediatricians to report cases of intussusception given the likely familiar. The study of the genotype could be decisive for or not to exclude the presence of a risk of invagination thus avoiding vaccination.

Disclosure of potential conflicts of interest

No potential conflicts of interest were disclosed.

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